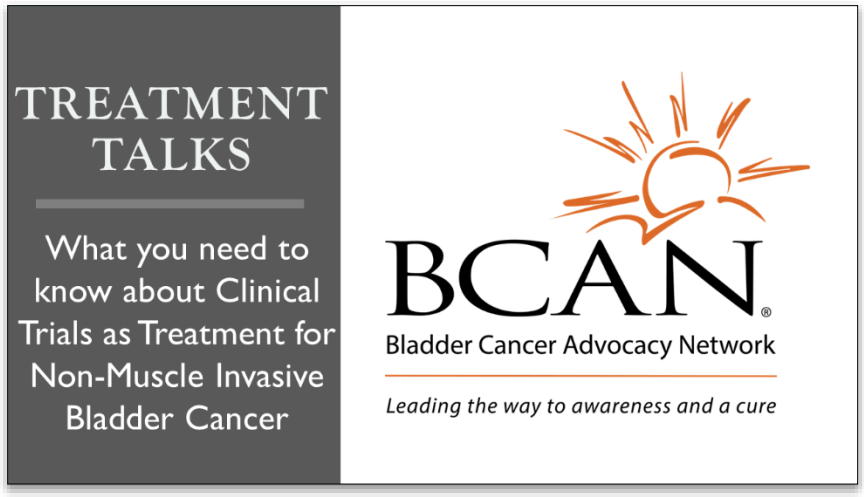

Stephanie Chisolm:

Welcome to Treatment Talk. What you need to know about clinical trials as an option to treat, excuse me, what you need to know about clinical trials as an option to treat non-muscle invasive bladder cancer. A presentation from the Bladder Cancer Advocacy Network. Treatment talks are a little different from our normal webinars. The goals of these programs are to increase patient understanding of existing and new treatments. And in this case of clinical trials across the spectrum of a bladder cancer diagnosis. We want to showcase patient questions to ask for empowering patient communication with your healthcare team if you're interested in a clinical trial. And we want to highlight some current treatment advances for bladder cancer, keeping in mind that no new advances get approved without clinical trials, which is the topic today.

So in today's program about clinical trials as a treatment option for non-muscle invasive bladder cancer, we are featuring Dr. Rian Dickstein from Chesapeake Urology where he's the director of their bladder cancer program and he's also the chief of urology at the University of Maryland. Welcome, Dr. Dickstein. It's a pleasure to see you.

Dr Dickstein:

Thanks for inviting me to talk this evening.

Stephanie Chisolm:

Great. And we've also invited Dr. Dickstein's patients, Stanley Wenocur, who is involved in one of Dr. Dickstein's clinical trials. So Stanley, it's a pleasure to have you with us as well.

Stanley Wenocur:

Pleasure to be here.

Stephanie Chisolm:

Great. Well, Dr. Dickstein, you're a community-based urologist treating mostly non-muscle invasive and muscle invasive bladder cancer patients. Tell us a little bit, what is the standard of care when a patient is diagnosed with non-muscle invasive bladder cancer? What's the usual treatment protocol that you're suggesting?

Dr Dickstein:

Sure. So typically we start with a TURBT, a trans urethral resection of the bladder tumor to get pathologic diagnosis. And we also do cross-sectional imaging to get staging evaluation. And then we categorize patients based on their level of risk. So we have a low, intermediate and high risk, and that will dictate the surveillance protocol and then the additional treatment that is needed for the patient. So for example, low-risk patients don't really need any additional treatment and we can surveil them relatively infrequently, whereas high-risk patients get a more intensive treatment to decrease the risk of recurrence and progression and keep a closer eye on their cancer.

Stephanie Chisolm:

So all of that comes from the material that's taken out with that TURBT where they go in and they scrape out that tumor. It goes to the pathologist who then provides a report of the cells that are found in that tumor?

Dr Dickstein:

Correct.

Stephanie Chisolm:

So clearly you're really interested in all these little nuances of a person's bladder cancer. Everybody has a different diagnosis. You do a lot of clinical trials there in the community, both at Chesapeake Urology and I think through your work at the University of Maryland. How did you get involved? Why are you involved in clinical trials? You're a community practitioner.

Dr Dickstein:

Yeah, I think my interest had started when I was in my training in residency and fellowship. I was exposed to a lot of clinical trials and I think the scientific inquiry was just really, really enticing for me. That's where it started. So just the desire and interest there, but some other things that have motivated me along the course of my career. Number one, are the challenges involved. Just this is a difficult population of patients to treat and trying to find new and innovative ways to help manage this disease is very interesting to me. Number two, is that it affords additional treatment options, so things that we don't otherwise have access to. So it gives me additional options to offer the patients, which is augmentations for them. And then the last is just the overall desire to do better than what we already have because we know that despite how good we are, we still have a number of failures and we always try to do better than what we've done historically.

Stephanie Chisolm:

This is great. So we have a standard care of patients who are diagnosed with bladder cancer based on what you just told us. Why do some patients with non-muscle invasive disease want to go into a clinical trial? What's common among those patients that want to, or if you're suggesting them, why wouldn't some patient want to do a clinical trial?

Dr Dickstein:

Some people think that they don't want to be a guinea pig, that this is going to be some trying something that has never been done before and it's obviously far from the truth. So I think number one is that if patients are not interested in the standard options, this affords them an opportunity to try

something that's different and novel. So they might get a therapy that might not be offered that's on the market and they might get to avoid some other therapies. For example, radical cystectomy, which is a very aggressive therapy that has significant morbidity. Hopefully they appreciate the importance of advancing science and the altruism of helping others. So the more we understand about these new therapies, the more we can help other patients as well. So I think there's secondary gains that are not necessarily specific to the patient, but hopefully they appreciate that.

Stephanie Chisolm:

So do all urologists talk to their patients about clinical trials?

Dr Dickstein:

Unfortunately, no. In smaller practices, they might not have the availability to access clinical trials and patients might have to go to academic centers. But in larger group practices, we are able to offer a lot of clinical trials. And so it's important for patients to ask about it and have access to it. Sometimes that material is not easy to find and I really appreciate Beacon's ability to disseminate that information For our patients.

Stephanie Chisolm:

We do list on our website bcan.org, all of the clinical trials that are currently open around the country that are recruiting patients. So if you're interested, you can always take a look there and you can even search by your diagnosis. So if you're non-muscle invasive disease, then you can go and search all the trials that are in your state or in the country. If you happen to have friends in a lot of locations, you could go and visit with somebody and do a clinical trial at the same time, if you're interested. So Stanley, welcome again. It's always so nice to see a patient that's on these calls. Tell us a little bit about your bladder cancer experience before we talk about why you got into a clinical trial.

Stanley Wenocur:

Well, my bladder cancer was identified the way I think many are, is I found some blood in my urine and I went to see the urologist and he said, there are a number of possibilities and had to take a look and said, no, this doesn't look right. And he did the cytoscopy and he did a TURBT, I guess. And he determined that in fact there was cancer and it was epithelial (urothelial), it was high grade epithelial (urothelial). So it hadn’t penetrated the muscle as I understand it, but as opposed to low grade, it was more at risk on being aggressive.

So the common treatments, at least that as I understood it, there was a treatment with BCG. And so I had one set of treatments with BCG and the biopsy after that showed four sites, three sites clear, one site's still cancerous. So then we were scheduled to do that again and COVID intervened. So what was supposed to have started in March 23rd, ended up being two months later. And that time I had the BCG treatments. And then afterwards the check turned up to be, it was very apparent there were bladder. In the bladder, there were numerous cancers all over the lining of the bladder. So they did a TUBRT cleaning that out. And I think they left or flooded it with, let me see, what is it?

Stephanie Chisolm:

Mitomycin?

Stanley Wenocur:

Mitomycin, yeah, thank you. Before they shut it, before they closed up.

And there I was and their recommendation was to do it again. And this was just Urology. And I said, well, that doesn't seem sensible. What are the alternatives? And so then they said, well, we have Rian Dickstein available. And so that's when we met.

But when we met, the cancer trial wasn't yet open and it was closed for a time being, for a short time, but it was closed at that point. And so I had to make some other preparation. So we began to look into what else. And Keytruda had come up on the market by then. And so I've made some arrangements to start treatment with Keytruda. And the one study that I saw, I said it was 40%, about 40% effective, wasn't a large study, but that's the data that I had. And the data with the chemical gemcitabine was 20% effectiveness. So I was worried, but I was about to start that treatment when I got a call from the cancer center at the University of Maryland that Rian was affiliated with and they said, we are now open. Do you want to talk to us about this? And so that was at one o'clock in the afternoon. At three o'clock I was down there to meet with them and that's when we began.

Stephanie Chisolm:

How did you work through whatever questions you might have had? Was there somebody on the clinical trial that you were assigned to that could explain it to you?

Stanley Wenocur:

Yeah.

Stephanie Chisolm:

How did you learn what was going to be addressed in the clinical trial and what your responsibilities were, being a patient in this trial?

Stanley Wenocur:

Yeah, that afternoon when we met with the doctor at the Cancer Center who was monitoring the patients in that trial. And so he explained what was expected of the patients and how this would work. I also met with the manager of the client, the trial manager, and she also explained what was supposed to happen and so on. And I came back again for another meeting and I had a big handout of all the materials and what was going to happen and exactly what the schedule was and what the protocol was and so on. So they explained it pretty carefully

Stephanie Chisolm:

And they wanted to make sure you knew what was going on, didn't they, before you signed? Didn't you have to do an informed consent where they told you all of these things?

Stanley Wenocur:

You have to do a informed consent. They have to tell you the risks.

Stephanie Chisolm:

I'm just asking because people want to know how do you do this. And were your questions answered that made you feel comfortable with the decision to go into the clinical trial?

Stanley Wenocur:

My questions were answered and Rian was very encouraging as well as an oncologist who was going to handle the Keytruda treatments in a different site in Columbia where I live, Dr. Ted Lee. So he was very clear too. Both were very clear that the cancer treatment and the cancer trial was worth trying. And it was clear from the data that they were getting good results. And in the back of my head was this image of removing the bladder, whatever that's called, the cys-

Stephanie Chisolm:

Cystectomy. Right. Radical cystectomy.

Stanley Wenocur:

Thank you. Dr. Dickstein introduced that to me. So that was in the back of my head and saying, I do want to avoid that. And I was in my eighties at that point.

Stephanie Chisolm:

Dr. Dickstein, what are some of the areas that people are doing research in doing these clinical trials that are helping to expand our knowledge about non-muscle invasive bladder cancer? Whether it's how to diagnose it or surveillance for it or how to treat it, what are some of the clinical trials that are common these days around the country, whether it's in a large academic hospital or in some of the larger urology practices?

Dr Dickstein:

Yeah, so historically there haven't been that many trials in the last couple years. There's been an explosion of trials. So luckily we've had a lot of different options for patients. So we have different groups. So I would say the first group is biomarker trials that can be used for evaluation of hematuria or even surveillance of bladder cancer. And most of them are urine biomarker trials. So they're pretty easy to do. Your patient just gives us a urine sample and they analyze the urine for whether it be proteins, DNA, RNA, different metabolites that are upregulated or higher in bladder cancer patients. And so those are really easy to do, easy for the patients, easy for us, and they help us understand, again, surveillance and evaluation of patients. So that's number one. Number two is treatment trials. And so we have different settings that we're evaluating treatments in.

So for example, we have BCG naive for high-risk patients. There was a Pfizer trial that we had done a couple years ago, the CREST trial, that's shortly going to read out, which we're excited about. We have treatment for intermediate risk, non-muscle invasive bladder cancer, so patients who have recurrent TA low grade disease, which is pretty exciting. There's a number of trials that are open that are going to be studying that field. And then most commonly right now is the BCG unresponsive setting, which is what Mr. Wenocur was a trial patient on.

And again, there's tons of trials in that space. There's the CG oncology trial, a new one coming up is enGene. The one that's people got really excited about is ImmunityBio with the QUILT trial. So there's a number of different trials out there. And then lastly, a trial that I'm really excited about that's been ongoing now for a while is a trial called CISTO, which is PCORI funded. So it's a patient-centered outcome trial, and it's looking at patients who have BCG unresponsive disease or who have failed BCG and decisions that they make regarding going on to radical cystectomy or having additional treatments, whether they be standard of care treatments or even clinical trial treatments. And to better understand how or why patients make the decisions that they do and going on with their treatment choices. So that's a pretty exciting trial that we're looking at right now as well.

Stephanie Chisolm:

So that doesn't actually involve them doing anything or having any particular procedure. It's just really evaluating from the CISTO perspective what the treatment options are and what patients are deciding to do about those treatment options?

Dr Dickstein:

It's simply a survey that patients fill out that give us their opinions or explanations for what the choices that they're making.

Stephanie Chisolm:

Full disclosure, that BCAN is a supporter of that particular trial. We meet on a regular basis with that trial. But again, that's one that is not necessarily a very invasive trial. So a lot of trials, there may be some patients who are enthusiastic because they want to make sure that nobody else goes through this down the road. And if they can stop bladder cancer in his tracks by participating in a trial, they would like to do that, but yet they don't get into a trial because there are inclusion criteria and exclusion criteria. Can you just give me an explanation? I think it helps people to understand why they are not eligible for a trial. What are some common things that would make you eligible or make you ineligible?

Dr Dickstein:

Right. It's a great question. So number one, it depends on what you're studying. And a lot of the trials are designed to study a very specific indication. So a couple things that factor into that. Number one is in order to get statistically significant values, you need to have a very specific population and a very high number of patients. So we have to account for that when we design the trial. Number two is, once the trial is accomplished, that data needs to be presented to the FDA, for example, in order for them to approve a drug to be able to be used on the market. And the FDA has very strict criteria as to when they make those decisions. And so we have to account for what the FDA is going to ask of us or ask of the pharmaceutical company, and we have to build that into our trial design as well.

So there's lots of different things that go into it. So that can be anything from the histology and making sure that it's appropriate histology, making sure that they've been treated appropriately in the past. So for example, if they have BCG unresponsive disease, you want to make sure that they got BCG, that they got that right amount of BCG, that the timing was appropriate for the failure of BCG or for the unresponsiveness of the BCG. So there's very strict criteria for some of these things that might exclude certain patients. You want to make sure that they're healthy enough to get the drug that they don't have any contra indications, so that they're not going to have any toxicities from the drug that they're going to get. So again, there's lots of different things that would factor into this decision.

Stephanie Chisolm:

So yeah, they want to make sure when push comes to shove and it goes before the magnifying glass of the FDA that they can't say, well, that patient had something else. And so that's partly why. So it does make it a little bit of a challenge. So what are some common questions, or Stanley, what were some questions you thought really helped you understand that that's what I wanted to do, I'm going to do this clinical trial? What are some common questions patients should ask?

Stanley Wenocur:

Well, I guess the main one for me was well, what are the alternatives? What's available? What are the alternatives to trying that? And the answer just made sense to me as it was clear that pembrolizumab by itself by itself was probably not going to be successful in many cases. And couple that with a chemotherapy agent, but that by itself wasn't going to be successful. So putting the two together just made sense to me to try them both.

Stephanie Chisolm:

And then your other alternative of not doing the clinical trial would be having your bladder removed, correct?

Stanley Wenocur:

Well, I guess we would've tried another round of BCG.

Stephanie Chisolm:

Okay. So another round of BCG.

Stanley Wenocur:

And if that didn't work, then I would be in the bladder removal business.

Stephanie Chisolm:

Yeah. Dr. Dickstein, you see a lot of people coming in and out of clinical trials. So what are some of the things you think patients should ask about?

Dr Dickstein:

Yeah, think that there's a number of different factors. I think number one is you want to know what the efficacy of the current therapies are, meaning what is the success rate of BCG, of pembrolizumab, of salvage intravesical chemotherapy and what we think that the efficacy might be of this, whatever the novel drug is, or combination of drugs that's being studied. So that's number one. Number two is like Mr. Wenocur said is, what are the alternatives? If we don't do the trial, what are the options? Number three is what are the toxicities? What are the bad things that could happen if I do do this trial or if I don't do this trial? You want to know about the intensity of the trial. Meaning, how many visits am I going to have? How often am I going to get this drug? How often am I going to be surveilled? And a lot of patients are coming from pretty far away, and so that's a pretty onerous burden on them to travel and to get that treatment and have to do that many visits and follow ups.

And so those are probably the biggest questions I would have if I were a patient, but that's what patients should ask. So I think those are probably the biggest ones to hit on.

Stephanie Chisolm:

Great. Okay. So you do all of this research, and clearly you're interested in doing clinical trials and encouraging some of your patients, but how do the clinical trials that you're involved in, how do they influence and guide or shape your recommendations for patients? because you're on these trials, are you more likely to recommend these newer treatments as they get approved Because hey, I was on that trial, I saw what it can do. Does that shape?

Dr Dickstein:

Yeah, it's a great question. I think that I definitely have a bias. And my bias as Mr. Wenocur pointed out, a lot of the standard of care treatments that we have, particularly in the BCG unresponsive setting is that that are not super effective. And so my bias is to push clinical trials as an option for patients because again, the goal and the hope is that we can do better than what we've already done. So I do have a bias to push the clinical trials. Now, the advantage of being an investigator on the trial is that you do get experience with the therapy. So your office staff gets to learn how to administer the therapy, they get comfortable with how it's dosed and even some of the side effects and how to manage some of the side effects. So it gets you a step up in terms of easy access to using the drug.

Stephanie Chisolm:

Sure. I think that that's certainly a big thing because in urology, in bladder cancer, so much of it is done surgically or intravesically. They put medication in the bladder and it's treated that way. But some of these newer agents, and in some ways it's like a fancy cocktail for bladder cancer where you're combining treatments like the trial that Stanley was involved in, where they're using an immunotherapy and chemotherapy because it helps synergize and build its effectiveness. It does require, because immunotherapy is typically given by infusion, you need to have a staff there. So I think that that's certainly a nice incentive from that perspective. You've already got people trained to do that, so that certainly makes it more valuable.

Stanley, quick question for you. In terms of the amount of time, the commitment that was required for you to be in a trial, was that ever an issue? Because some patients might think, well, this is too long of a time period or something. Was that an issue for you?

Stanley Wenocur:

Well, I'm probably fortunate because I retired. I'm retired as a professor at the University of Maryland, so I was retired by then and time wasn't an issue. I was doing things in my retirement, but it was my own time, so it wasn't really an issue. It is a bit of a drag though, if you have a lot of sessions to go to, but you do it.

Stephanie Chisolm:

You have to fit your life activities, the things that you might be doing with family and friends or travel or whatever into, well, I've got to be back at Dr. Dickstein's clinic because I need to have a follow up or something like that.

Stanley Wenocur:

That's right.

Stephanie Chisolm:

But generally is not too unmanageable in most cases, right?

Stanley Wenocur:

I would think not. I think it's pretty manageable, but I don't know enough about other clinical trials.

Stephanie Chisolm:

Right. Dr. Dickstein, here's a question for you. If somebody were to say, yeah, I want to be in a clinical trial, and then they said, this is overwhelming, this is too much work, I can't keep coming back for all of this testing and all these other things, what happens if they decide they don't want to do it anymore?

Dr Dickstein:

Yeah, the nice thing is that they always have the ability to stop at any given time and they can withdraw from the trial. And that means a number of different things. That can mean that you just don't get the drug, but we still follow you. And that can means that you just stop altogether. So there's always the ability to opt out if at any point it's not going well. Or for example, if they have an adverse event that prohibits them from getting the treatment anymore.

Stephanie Chisolm:

Adverse events are the medical term for side effects basically, they're not wanted effects of what's going on. So that's generally what we're talking about with adverse events, because not everybody uses that terminology. So other than that, I think we've covered a lot of really good ground. Let me ask another question, going back to a standard misbelief, I think a lot of people remember what their high school science class said, teaching them about experiments, and they may be reluctant to be in a clinical trial because they don't want to get the pink sugar pill. They don't want to get the placebo, they know about the placebo, and that's in a real experiment. But in a medical clinical trial, do patients get placebos with cancer?

Dr Dickstein:

They can. So we have different types of trials. So in general, there's phase one, phase two, phase three, and then sometimes we have phase four. So phase one is typically a dose escalation trial. That's where we try and identify an appropriate dose of the novel drug that we're doing or using, I'm sorry. And so they get the drug and they just might get different doses. And we have to find what the optimal dose is in terms of efficacy and toxicity. Number two, I'm sorry, phase two trials typically are looking for some signal. You want to check and see if the drug really actually does work the way we think it does. And then once we have some signal that it's really working, then we get to phase three trials. And phase three trials are really our gold standard trials. Those are trials that for the most part, well, I should say some of them can be drug versus standard of care.

Some of them could be drug versus other drug, but those are the pivotal trials that we really use to prove that the drug is doing what we think it should be doing and is very effective. And then phase four is once the trial is approved by the FDA, and it's been being used out in the real world, we check to see that it's doing, again, what we thought it was doing on the earlier phase trials. And so depending on what type of trial you're on, you might get drug versus placebo, but many times we are getting just drug. And so that's an important question to ask when you're being presented with a trial.

Stephanie Chisolm:

So it's drug versus standard of care, which would be some of the other treatments, like in this case it would be more BCG?

Dr Dickstein:

Yeah. And I would say that, again, it depends on what we're looking at, but a lot of the BCG unresponsive trials, which are the majority of them right now, are single arm trials, meaning that they get patients get the drug and there's no placebo. It's because they're very difficult to enroll, and it's not

necessarily ethical not to give no drug. And so we have to weigh those balances of getting the best data we can, but being ethical in terms of our treatment.

Stephanie Chisolm:

Right.

Stanley Wenocur:

Yeah, it would be unethical.

Dr Dickstein:

Correct.

Stanley Wenocur:

That's right, it would be.

Stephanie Chisolm:

So before we switch over to some questions from participants, Stanley, let me ask you, were there any lessons that you learned or challenges from your experience enrolling, in participating in the trial that you want to share with the participants on this call?

Stanley Wenocur:

Well, every trial is a little bit different and the places where they're administered are a little bit different. In my experience with the Tate Cancer Center, I had to get used to, but this may be typical, I had to get used to the amount of time that it took to do the things. I was getting two kinds of an infusion into the bladder of a chemotherapy agent. And then you had to hold that for an hour, and so you at least were tied up for an hour. And then I was getting in the shot in the eye, the infusion of the Keytruda, and that was rather quick. It was usually about a half an hour. But in between all of that, people are busy, you're in a cancer center, there are other patients. They had some staff shortages. So you really had to set your sites on saying, well, this is the day that I'm going to have this treatment, and I can't worry about the time too much. I've just got to be able to deal with it.

The other main issue that I had with the cancer treatment and the administration of it wasn't a problem with the drugs and there was no problem with the Keytruda, but there were problems with the bladder infusion. Catheterization was not familiar to the nurses. They were not experienced. And so some of that was pretty unpleasant. The head nurse did know what she was doing, and when she took over that work, and she unfortunately died tragically in a car accident and died. And then the woman, the nurses who replaced her were very careful. And though, I don't know if they were familiar with catheterization, but they were really good nurses. So it worked just fine. There was questions about having the right catheter size. I had infusions into the bladder with the BCG and then in that doctor's office, and it was two minutes and it was nothing. And here was a whole production the first time.

Stephanie Chisolm:

The general gist, I guess is, did you get those questions and concerns addressed? Were they able to do that because they usually have a lot of people involved in the clinical trial?

Stanley Wenocur:

Well, and as far as I understand it, in that center there were two people involved in this particular trial. I never saw the other person. I don't know who it was, it was a man, that is all I know. They did address them. Eventually they did address my concerns. So in that sense, it was fine. The other thing that happens is that for me at least, and maybe it's different for other people, but I found myself worrying about side effects. And I did feel some side effects and it's hard to know. And particularly in my case, hard to know because I'm an elderly person, I had to believe, at least on the outside, my body says I'm elderly. So whether the deterioration that I might be experiencing, let's say having trouble walking, was really related to the Keytruda because it says, well, could be a side effect or related to the fact that my own spine is degenerating. And so I've got those kinds of problems.

Most of the side effects that I experienced were minor, headache, stomach ache, fatigue, that was fairly common. And trouble walking, which again, I say was not clear whether the cause was the treatments or the cause was my own degenerative body. But the one side effect that seems to have stuck is itchiness. That was never resolved. There was no cease, no solution to it. Benadryl was not the answer. And Benadryl is not a, if you're elderly, you don't want to be taking Benadryl particularly.

Stephanie Chisolm:

But you felt like you got good care and they were able to address some of those side effects, and-

Stanley Wenocur:

Sure.

Stephanie Chisolm:

... you were encouraged to report them, right?

Stanley Wenocur:

Sure. Oh sure. And I would say for anybody going into a clinical trial, you ought to keep a calendar and a record of your experience, which I did. But I think it's a good idea because then you can look back at it and you could remind yourself as for what happened and what happened the last time and so on.

Stephanie Chisolm:

What you might not think in two weeks was important might have been an important thing if you don't remember when you go back in.

Stanley Wenocur:

That's right.